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IMPACTS OF CLIMATE CHANGE ON HUMAN HEALTH: FUTURE RESEARCH DIRECTIONS

Warren T. Piver and Samuel H. Wilson
National Institute of Environmental Health Sciences
P.O. Box 12233
Research Triangle Park, NC 27709 USA

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SUMMARY

Impacts of climate change on human health may include an increase in heat and air pollution related morbidity and mortality from cardiovascular and respiratory diseases and an increase in infectious diseases, particularly vector and water borne diseases. In addition, increased exposures to shorter wavelength ultraviolet radiation (UV-B) as a result of depletion of stratospheric ozone may cause an increased incidence of melanoma and non-melanoma skin cancers, cataracts and other ocular diseases, as well as immune system dysfunction and increased susceptibility to opportunistic viral and bacterial diseases. Research agendas developed from two workshops on these topics are presented. Along with recommendations to identify risk factors and mechanisms for these diseases in human populations, it was strongly emphasized that there needed to be greater coordination between biomedical scientists and climate scientists. Climate models should provide data and predictions of climate variables that are sensitive to time and regional geographic scales needed to assess the impacts of climate change on human diseases and to develop better intervention and preventive strategies.

INTRODUCTION

The Intergovernmental Panel on Climate Change (IPCC) has projected that atmospheric concentrations of CO_2 could double in the next 50 to 100 years (Houghton et al., 1996). Because of the greenhouse effect, a doubling of atmospheric concentrations of CO_2 could result in an increase in average global ambient air temperatures of 1 to 3°C and a sea level rise of 0.2 to 0.8 m. In addition, because approximately 65% of atmospheric concentrations of CO_2 are from the combustion of fossil fuels, increasing concentrations of CO_2 could also be accompanied by exposures to higher concentrations of air pollutants, particularly in large urban areas. An

increase in surface air temperatures could be accompanied by a greater frequency and duration of heat waves. Because heat waves often occur in large metropolitan areas, these large cities could experience an increase in the incidence of heat related morbidity and mortality (Kalkstein, 1993; McMichael et al., 1996). Increasing temperatures could also result in an increase in vector borne diseases such as malaria (Carcavello and Caras, 1996; Epstein, 1994), and water-borne diseases such as cholera (Colwell, 1996; Epstein, 1992; 1994) because the geographical areas in which these diseases occur could be expanded to higher latitudes above and below the equator and to higher altitudes in equatorial latitudes. In addition, depletion of stratospheric ozone could result in greater exposures to shorter wavelength UV radiation and a resulting greater incidence of both non-melanoma and melanoma skin cancers (Kripke, 1994), cataracts and other ocular diseases (McMichael et al., 1996).

Heat waves are characterized as periods of prolonged high daily average temperatures, T_{av}, high maximum and minimum temperatures, T_{max} and T_{min}, high relative humidities, and stagnant air movement. In addition, heat waves often have high air pollutant concentrations. During a heat wave, hot days are often followed by hot nights. These conditions produce a high degree of heat and air pollution stress, particularly for the elderly and other individuals susceptible to cardiovascular and respiratory problems. During heat waves, combined exposures to some or all of these factors often occur either on the same day or within a short time of each other. Prolonged periods of higher daily maximum and minimum temperatures and greater rainfall amounts in latitudes above and below the equator and at higher altitudes in equatorial latitudes, are conditions that favor growth and activity of insects that are vectors for the transmission of infectious diseases such as malaria, dengue fever and Chagas' disease.

In September 1997 and November 1998, two workshops were convened to consider the research agendas for assessing the impacts of climate change on human health. In the first, the impacts of climate change on the spread of vector-borne and other infectious diseases were the topics for consideration by workshop participants (WAG, 1997). In the second, the impacts of climate change on greater exposures to thermal and air pollution stress and greater exposure to shorter wavelength ultraviolet radiation (UV-B) as a result of depletion of stratospheric ozone, were the topics for consideration by workshop participants (WAG, 1998). The results of these two workshops are summarized to provide a starting point for the development of global research agendas to provide biomedical information to assess the impacts on human health of higher ambient air temperatures in all latitudes, potentially greater exposures to thermal and air pollutant stress, greater exposures to UV-B radiation as a result of

depletion of stratospheric ozone and the emergence and spread of infectious diseases into temperate climatic zones above and below equatorial tropical climate zones.

HEAT AND AIR POLLUTION STRESS

Heat stress is the result of prolonged exposures to high ambient temperatures. If temperature regulating processes in the body are not able to maintain thermal equilibrium, core body temperatures can rise above normal body temperatures of approximately 37°C. The body's response to increasing thermal stress produces a strain on the cardiovascular system and other physiologic systems that are trying to return core body temperature to normal levels to maintain thermal equilibrium. Because the body's response to heat stress involves multiple organ systems and physiologic functions, the pathological sequences of heat stress may not only be attributable to increasing core body temperature, but also to the collapse of multiple physiological control systems, such as those regulating fluid and electrolyte balances. Increased mortality observed during heat waves is primarily from cardiovascular and/or respiratory causes of death (Jones et al., 1982). The cardiovascular strain induced by the systemic response to heat stress can combine additively or synergistically with increased respiratory difficulty from chronic obstructive pulmonary diseases such as emphysema or asthma.

Figure 1 illustrates the possible effect of a temperature increase of 4°C on the mean maximum daily temperatures, T_{max}, during the month of July for Chicago and Tokyo. In this plot, the actual distributions of T_{max} for July 1995 for Chicago and Tokyo are shown. Superimposed on these distribution curves for the two cities are curves shown as dashed lines that show how the mean for July maximum daily temperatures can be shifted by 4°C for both cities. The vertical line at a temperature of 35°C is used to determine the probability of exceeding this temperature for both cities for the July 1995 distributions and for the situation in which the means have been shifted by 4°C. If the standard deviations for T_{max} for both cities are held constant at SD = 3.67°C for Chicago and SD = 4.09°C for Tokyo, the probability that T_{max} will exceed 35°C for Chicago could increase from 0.057 to 0.312, and for Tokyo from 0.041 to 0.223. These increases represent significant increases in the number of days during the warm summer month of July in which the populations of these two cities could be exposed to very high T_{max}.

Classic heat stroke occurs mostly in the elderly, the young and the chronically ill, especially people with cardiovascular diseases (Dematte et al., 1998 ;Jones et al., 1984). Exertional heat stroke is more likely to occur in healthy people who have been working, playing or exercising too hard

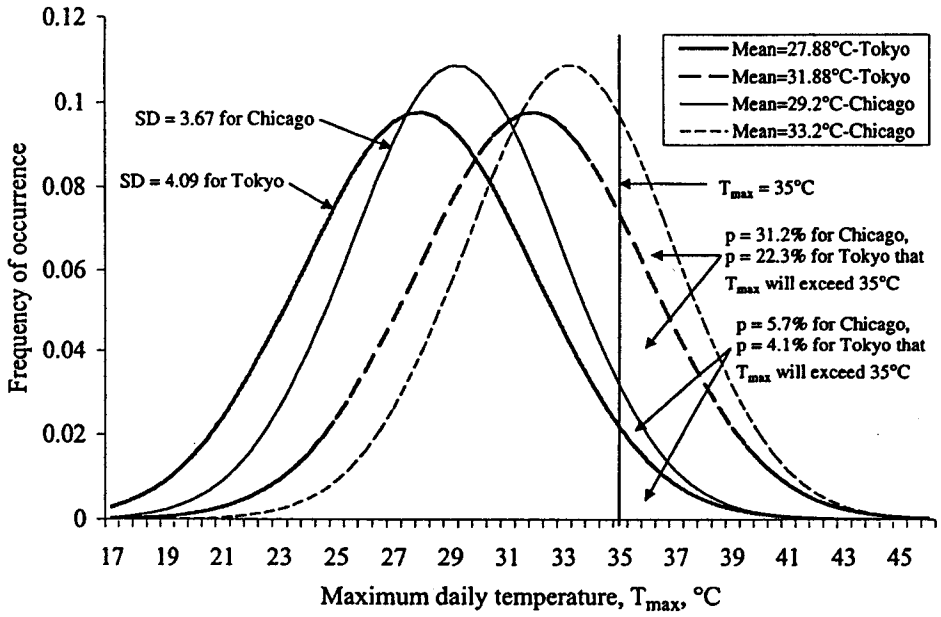

Figure 1 Distributions of T_{max} in July for Tokyo and Chicago. Graphs show distributions for July, 1995 for both cities and the distributions if the mean T_{max}'s are increased by 4°C. The standard deviations (SDs) for both distributions are held constant when the mean T_{max}'s for both cities are shifted by 4°C.

when temperatures and relative humidities are high. Figure 2 plots data on the daily average number of heat stroke emergency transport cases/million for age 65+ males and females and the daily average T_{max} for Tokyo for July and August 1980 and 1995. These data were obtained from the Japan Environment Agency and the Tokyo Emergency Office. Plotted in this manner, Figure 2 illustrates the very close correlation between daily average maximum temperatures, T_{max}, and the average daily number of heat stroke emergency transport cases/million for 65+ males and females in Tokyo for the July and August from 1980 to 1995.

In developing research needs for impacts of thermal and air pollution stress on human health, Table 1 is composed of three columns. In the first are potential risk factors. The second column identifies health impacts as a result of exposures to these risk factors, and the third column identifies biomedical and climatological programs that are needed to assess the health impacts of combined exposures to higher temperatures, relative humidity and air pollutant concentrations.

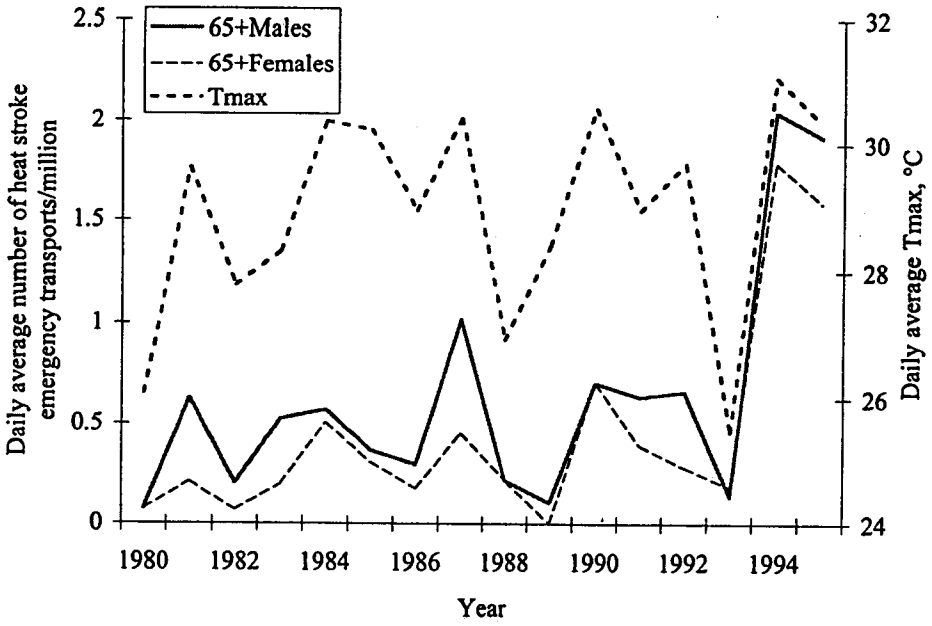

Figure 2 Daily average number of heat stroke emergency transport cases/million for age 65+ males and females, and daily average maximum temperature, T_{max}, Tokyo, for the months of July and August, 1980-1995.

Because multiple climate and environmental factors can affect the systemic response to heat stress, combined exposures to all climate and air quality conditions that can exacerbate or ameliorate the response must be considered when assessing the impacts of climate change on health effects of heat stress morbidity. Data collection and analysis for heat stress

Table 1 Research needs for impacts on human health of thermal and air pollution stress

Risk factors	Health impacts	Research needs
Stressful weather conditions such as higher T_{max}, T_{min}, T_{av}, relative humidity and air pollutant concentrations; stagnant air masses and prolonged exposures to stressful thermal and air quality conditions; age, gender and pre-existing diseases	Increased heat stroke (classic and exertional), cardiovascular and respiratory morbidity and mortality	Assessments of combined exposures to climatic and environmental factors; patho-physiological mechanisms of response to heat and air pollutants; identification of biological markers of heat stress, e.g., heat shock proteins; climate models based on health sensitive time and location scales

morbidity, however, are not done routinely and need to be improved. In many instances, hospital admissions may not appear to be consequences of thermal stress because they are attributable to underlying patho-physiological conditions, such as cardiovascular disease, rather than the strain associated with thermal stress. Increases in non-fatal illnesses and decreases in functional capacities associated with heat stress and concomitant and simultaneous exposures to air pollutants may represent a large societal cost that can be decreased by appropriate preventive actions.

To assist in this process, climate models must include more consideration of health critical variables such as air pollutant concentrations, along with a consideration of temperatures, wind speeds, wind directions and relative humidity. In addition, the time scales for changes in these variables and geographic scales in model predictions must be more sensitive to the times frames in which these diseases occur and provide a more sensitive indication of where these diseases are occurring at higher than normal frequencies.

Underlying these needs for inclusion of multiple risk factors for heat stress and better predictive climate models for exposure assessment, is the need to examine in more detail the patho-physiological mechanisms of responses by cardiovascular and other systems as a result of thermal stress. Identification of biomarkers of heat and air pollution stress would make it possible to identify vulnerable populations.

STRATOSPHERIC OZONE DEPLETION AND GREATER EXPOSURE TO UV-B RADIATION

Stratospheric ozone filters out biologically harmful ultraviolet radiation in sunlight in the region from 200 to 320 nm (UV-C and UV-B regions). Depletion of stratospheric ozone has occurred because of the widespread use of chlorofluorocarbons (CFCs). These chemicals have been widely used as solvents, fire retardants and refrigerants and are also very effective greenhouse gases when present in the troposphere. The CFCs are chemically unreactive in the troposphere. However, because of their very long half lives and chemical unreactivity in the troposphere, they gradually migrate into the stratosphere where they are photo degraded by UV radiation in sunlight. The reaction products of the photo degradation of the CFCs reacts with ozone in the stratosphere, depleting its concentration and lessening the capacity of stratospheric ozone to filter out biologically harmful UV-B and UV-C radiation from sunlight. Depletion of stratospheric ozone has been greatest over Antarctica (Stolarski et al., 1992) and in the Arctic circle as a result of the eruption of Mount Pinatubo in 1991(Wilson et al., 1993). However, there have also been noticeable

depletions of stratospheric ozone in mid latitudes above and below the equator (Blumthaler and Ambach, 1991).

The 1987 Montreal Protocol and subsequent amendments represented a concerted international effort to eliminate the release of the CFCs by curtailing their manufacture and use. A 1998 assessment (WMO, 1998) reported that total combined abundance of ozone-depleting chemicals in the troposphere peaked in 1994 and was slowly declining. However, the combined abundance of ozone depleting chemicals in the stratosphere is expected to peak in 2000. Even so, the gradual reversal of depletion of stratospheric ozone and a return to levels before large scale depletion began, is not expected to occur until about 2050. The uncertainties and human health concerns about the return of stratospheric ozone concentrations to levels that are effective in filtering out biologically harmful UV-B radiation in sunlight at all latitudes, are magnified because the effects of UV-B on human health appear to be cumulative. For some effects there are long latencies from the time that exposures occurred until effects are observed.

Table 2 Research needs for impacts on human health of greater exposure to UV-B radiation

Risk factors	Health impacts	Research needs
Depletion of stratospheric ozone; pigmentation; opportunistic viruses and bacteria and compromised immune function; age gender, and pre-existing conditions	Increased incidence of melanoma and non-melanoma skin cancers; cataracts and other ocular diseases; dysfunction of systemic and cutaneous immune systems	Models to predict ground level exposure intensities of UV-B radiation; mechanisms of skin cancers induced by UV-B radiation; effects of UV-B on the systemic and cutaneous immune systems and the relationship to cancer induction; bio- markers of recent and cumulative exposures; identify action spectra for specific effects; epidemiology of NMSC; combined effects of UV-B and environmental factors

Table 2 has a similar format as Table 1 and outlines the risk factors, diseases and research needs associated with greater exposures to UV-B radiation. Probably the most important data for assessing the impacts of exposure to UV-B radiation are reliable baseline measurements of UV-B exposures at all latitudes. Before assessments of the impacts of greater exposure can occur, it is essential to know what exposure levels are presently. It is also essential to have biological markers of short term and cumulative exposure to UV-B radiation. The relationship between the abundance of these biological markers in circulating body fluids and observed short term and cumulative effects with long latencies will be very important in sorting out mechanisms for UV-B induction of these diseases. In addition, there are different wavelengths within the UV-B region that are more effective than others for causing specific biological effects. Thus the

quantitative relationships between UV-B dose and a physiological effect varies with the distribution of wavelengths in the UV-B dose. A plot of the relative efficiency of each wavelength to produce a particular effect is called the "action spectrum" for that effect. An example of the wavelength dependency of UV induced skin cancers is given de Gruijl and van der Leun (1994).

The known effects of UV-B on the eye include short-term inflammatory reactions from acute exposure, snow blindness (photo-kerato-conjunctivitis) and long-term damage to the cornea and lens (cataracts) from chronic exposure. The mechanisms by which long-term exposures to UV-B initiates and/or enhances the long-term processes that result in vision impairing endpoints such as cataracts are not established. Sunglasses, especially those that wrap around the eye and protect it more completely from side exposures to UV-B, are effective in preventing short-term inflammatory effects and longer term damage to the cornea and lens.

The mechanism by which UV-B exposure induces skin cancers is also incomplete, even though many stages in this process have been identified (Kripke, 1994). For example, it has been demonstrated that damage to melanocytes in the skin, initiates the progression of changes leading to melanoma. Melanomas are more likely to develop on skin areas that are subjected to intermittent high doses of sunlight such as the middle and lower back, whereas the squamous and basal cell carcinomas that characterize non-melanoma skin cancers NMSC, are likely to appear in areas of maximal exposure over long periods of time such as the face and the backs of ears. The steps involved in progression from an initially damaged skin cell to a rapidly growing or metastasizing malignancy are ill-defined, as are the mechanisms for potential contributions of genetic and environmental factors.

Suppression of the immune response by UV-B radiation has been well established in laboratory animal studies but the mechanisms are not understood completely (Kripke, 1991). One possibility involves damage to the Langerhans cells in the skin, which are important in antigen presentation and subsequent activation of T lymphocytes. UV-B exposures simulates the production and release of immunologically active substances from cells in the skin, including some factors that can suppress immune response. These studies in mice raise the question of whether exposure to UV-B can also impair host defenses against infectious diseases. Studies in mice have shown that exposure to UV-B can increase the severity of certain infectious diseases, but the possibility of this type of response has not been demonstrated to occur in humans.

Finally, it is very important to collect incidence data on ocular diseases and non-melanoma skin cancers. Both of these diseases are usually treated in physician's offices and are not reported adequately or accurately.

Without more complete reporting of data on these diseases, it will be difficult to determine if the rates of these diseases are increasing or decreasing or if there are geographic or other risk factors for these diseases.

VECTOR-BORNE AND OTHER INFECTIOUS DISEASES

A proposed research agenda for infectious diseases is given in Table 3. Insects and microbes generally strive in warm, moist conditions. When these climatic factors are coupled with poor sanitation and hygiene, along with over-crowded living conditions, the spread of contagious and vector-borne infectious diseases is usually very high and many people are infected. For contagious diseases, the infective agent spreads directly from person to person as in cholera. Warmer sea temperatures from El Niño events (Knutson and Manabe, 1994; Tett, 1994) make it possible for large phytoplankton blooms to occur for extended distances along continental coastlines. These phytoplankton blooms offer excellent habitats for the survival of infectious bacterial diseases such as cholera. The appearance of these extended phytoplankton blooms have been linked with cholera outbreaks in 1991 along the entire coast of Peru and along the entire coast of Bangladash in 1994 (Colwell, 1996).

In vector-borne infectious diseases, an intermediate vector organism such as a mosquito, fly or snail, is required to transmit the infectious parasite between humans. Approximately 2.2 billion people are at risk of contracting malaria and approximately 600 million people are at risk of contracting schistosomiasis (McMichael et al., 1996; WHO, 1993; 1996). Most of the people who are at greatest risk of disease live in the tropical climate zones of Africa, Asia, South and Central America. An estimated 2 million people die from malaria each year including about a million children. Temperatures between 20°C and 30°C and relative humidities of at least 60% are optimal for malaria-transmitting mosquitos to survive long enough to acquire and transmit the infection. Small increases in daily maximum and minimum temperatures can enhance the rate of passage of the parasite through its mosquito-borne incubation and development stage and can reduce the time for this process from about 3 weeks to as little as one. Janssen and Martens (1996) and Martens (1995) have developed evolutionary models for malaria and schistosomiasis to predict how climate change can increase the rates of disease in areas that are already heavily infected and affect the spread of these diseases into latitudes above and below the equator.

The geographic distributions of many other protozoal parasites are closely correlated with ambient air temperature. These include trypanosomiasis (sleeping sickness), filariasis (elephantiasis), onchocerciasis (river blindness), leishmaniasis, hookworm, guinea worm and various

Table 3 Research needs for the spread of infectious disease as a result of climate change

Risk factors	Health impacts	Research needs
Increasing air and water temperatures, relative humidity; prolonged periods of conditions favorable for growth and survival of infectious disease vectors in more northern and southern latitudes and at higher altitudes in temperate latitudes; poor hygiene and sanitation; over-crowding	Greater incidence of vector-borne diseases such as malaria, dengue fever and schistosomiasis; and water-borne diseases such as cholera; the spread of these diseases into areas with low levels of disease, resistance and incidence	Better climate models to quantify disease vector movement and the changing patterns of ocean temperatures along continental coastlines; new vector control agents that do not degrade the environment; new treatments for resistant forms of vector-borne diseases

tapeworms. Likewise, the distributions of many vector-borne viral diseases such as dengue and yellow fever are affected by air and surface water temperatures because they are spread by the *Aedes aegypti* mosquito (Haines et al., 1993).

The dynamics of survival and transmission of many water and vector-borne diseases are closely linked with the dynamics of local ecosystems. Climate models that are being developed to predict the effects of climate change on ecosystem dynamics must take these factors into account. Variations in rainfall and temperatures have a very large impact on the survival and activity of insect vectors for infectious diseases and the models must be designed to predict regional changes in these variables that reflect the time scales required for insect vectors for infectious diseases to mature and transmit their parasites to human hosts.

Finally, there is a need to develop new treatments for these diseases. Efforts to eliminate and control insect populations have been successful in the short run, but have also produced populations of insects that are much more resistant to chemical controls, and have produced forms of the diseases which are much more resistant to presently available treatments. Not only is it necessary to develop new treatments for these diseases, but it is essential to develop new forms of insect control that control the spread of the vector without destroying the regulatory mechanisms of ecosystems to control insect populations.

SUMMARY

For all three topics on the impacts of climate change on human health, it was emphasized that there was a strong need to link health impacts to climate and environmental factors. In addition, for the models that are being developed to simulate climate change to be useful for

biomedical researchers, the model output must provide changes in climatic and environmental factors for specific locations and region, and must provide changes in these variables that are consistent with the time scales required for these diseases to occur. For heat related diseases, the time scales would be days, whereas for insects that are infectious disease vectors, the time scale could be weeks to months. In addition, many of these diseases are seasonal in nature, and climate model output should also provide this type of seasonal variability over periods of 10 to 15 years. For the assessments of the impacts of climate change on human health in all regions of the world to be as accurate and credible as possible, the preservation and unrestricted access to climatic, air quality, UV-B radiative intensities and spectra at ground level and human health response data are essential.

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